UK Small Animal Disease Surveillance Report with a focus on pruritus and coagulase positive staphylococci.

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ABSTRACT

Presentation for pruritus comprised 6.5%, 3.6% and 2.0% of canine, feline and rabbit consultations, respectively. The most commonly prescribed pruritus treatments were topical antimicrobials for dogs (33.6% of consultations) and systemic glucocorticoids for cats (53.5%). Sixteen percent of 176 coagulase positive staphylococci (CoPS) isolated from canine diagnostic samples were sensitive to all tested antibacterial classes; multi-drug resistance (resistance to three or more antibacterial classes) was found in 6.9%.

Report summary

This report is the third in a series by the Small Animal Veterinary Surveillance Network (SAVSNET). In the first two sections it focusses on surveillance for pruritic skin disease in veterinary practice and for laboratory-confirmed diagnosis of coagulase positive staphylococci (CoPS), which are frequently involved in skin disease and pruritus, particularly in dogs. A third section presents a brief update on surveillance for gastrointestinal and respiratory disease, the syndromes analysed in previous reports. This is followed by an update on one important and emerging antibiotic resistant CoPS, methicillin-resistant *Staphylococcus pseudintermedius* (MRSP). The final section aims to summarise some recent worldwide developments in companion animal infection, namely Aujeszkys disease, rabbit haemorrhagic disease, babesiosis and Lyme disease.

Syndromic surveillance of pruritus

Pruritus, or itch, is defined as an unpleasant sensation that provokes the desire or reflex to scratch. It is common in many types of skin disorders. It is often accompanied by red, inflamed areas of skin and may lead to pyoderma. Pruritus is commonly associated with flea allergy and other allergic skin diseases. Here we describe animals presented to 217 veterinary practices (459 premises) between 1st January 2014 and 30th June 2016 with a primary problem of pruritus. The data were obtained from the Small Animal Veterinary Surveillance Network (SAVSNET). A detailed description of the methods used by SAVSNET to capture electronic health records (EHRs) may be found elsewhere (Sánchez-Vizcaíno et al., 2015).

In total, EHRs for 1,816,816 consultations were collected (including repeat consultations for the same animal), of which 70.0% were from dogs, 26.1% cats, 1.4% rabbits, 1.2% other species and 1.3% species unknown. Presentation for pruritus, as indicated by the veterinary surgeon's categorisation, comprised 6.5%, 3.6% and 2.0% of canine, feline and rabbit consultations, respectively. Short questionnaires relating to the anatomical location of the pruritus, the diagnostic tests planned and treatments recommended (Sánchez-Vizcaíno et al., 2015) were completed for 19,515 animals (15,527 dogs, 3,535 cats, 92 rabbits, 233 other species and 128 species unknown) based on a single questionnaire randomly administered to a proportion of these pruritus patients. A substantial proportion of dogs (19.5%) and cats (18.1%) were presented after a long history of illness (over one year). Diagnostic tests were planned in 21.8% of dogs and 25.2% of cats with pruritus, with cytology (5.9%) and skin scrape (3.8%) being most common in dogs, and hair pluck (3.1%) and adhesive tape strip (2.9%) the most common in cats. Microbial culture was planned in 3.0% of dogs and 1.4% of cats. The most frequent location of pruritus was ears (44.4%) and feet-limbs (26.5%) in dogs, and in cats, the dorsal body (46.4%) and face (28.9%). The results related to the treatments are shown in Table 1.

The spatial distribution of the relative risk for pruritus was evaluated in dogs and cats in England and Wales for each season of the year (Figure 1). Estimates for Scotland and Northern Ireland are not included because geographical coverage in these areas is currently limited. Animals were considered as "cases" if, during the season assessed, they presented for pruritus on one or more consultations. The spatial variation of the relative risk for pruritus throughout England and Wales was smoothed using a kernel smoothing method. The relative risk of dogs being presented with pruritus was estimated as the ratio of kernel-smoothed intensities (i.e. mean number of events estimated per unit area) of dogs presented with pruritus (cases) compared with all dogs presented for a cause other than pruritus (controls); the same approach was conducted for cats. Estimations were made using a grid cell of 5 km and a bandwidth of 50 km.

In dogs, many zones of increased relative risk were identified. Most areas appeared transient, although some areas in north Wales, north-west, north-east and south-west England seemed to have a higher relative risk throughout the year. In contrast, the picture in cats appeared more stable, with lower numbers of zones at high relative risk for pruritus compared with dogs, with winter having no zones of the highest relative risk. Together, these data reaffirm the different pattern of presentation for pruritus between cats and dogs, and suggest that the relative risk for pruritus varies spatially and temporally. It should be noted these zones may not equate to outbreaks; SAVSNET is currently developing models to allow outbreaks to be identified.

Laboratory-based surveillance of coagulase-positive staphylococci

Although there are a large number of species of coagulase-positive staphylococci (CoPS), the two most clinically relevant are *Staphylococcus aureus* (SA) and *Staphylococcus pseudintermedius* (SP) (Bannoehr and Guardabassi, 2012), with SP being most common in companion animals (Ruscher et al., 2009). Despite the emergence of meticillin resistance in both SA and SP (MRSA, MRSP – see section below), there have been no attempts to form on-going surveillance for CoPS in companion animals in the UK. SAVSNET collates anonymised results of clinical sample testing in diagnostic laboratories including antimicrobial resistance testing. Here we describe the phenotype of 184 canine CoPS isolates. Although SAVSNET receives antibacterial resistance data from several laboratories, both the complexity of these data, and the differences in formatting between laboratories, currently limit our ability to compare the results from more than one laboratory. Therefore this first summary is limited to an analysis of those data received from one laboratory during 2015.

CoPS was frequently isolated with other bacterial species; 21.3% also contained *Streptococci spp.*; 7.1% *Pseudomonas aeruginosa*; 3.8% *Escherichia coli;* 2.2% *Proteus spp.;* 2.2% *Pasteurella multocida;* 1.1% *Enterococcus spp.,* and 0.5% coliforms. A total of 176 CoPS (95.7%) had undergone further sensitivity

analyses, with 28 (16.0%) displaying sensitivity to all tested antibacterial classes, 135 (77.1%) displaying resistance to one or two antibacterial classes, and 13 (6.9%) with resistance to three or more classes (multi-drug resistant, MDR). Resistance seemed particularly prevalent for polymixin (polymixin B) and extended penicillin (amoxicillin) classes where 100.0% and 69.8% of tested isolates displayed resistance respectively (Table 2). In contrast, amoxiclav and 1st/2nd generation cephalosporin resistance was infrequent. Of the 13 MDR isolates, 10 displayed resistance to three antibacterial classes of which lincosamide-macrolide-extended penicillin resistance was most frequent. The eleventh isolate displayed aminoglycoside-polymixin-fluoroquinolone resistance. Two further isolates displayed resistance to five antibacterial classes; lincosamide-polymixin-fluoroquinolone-amphenicol-1st/2nd gen. cephalosporins, and aminoglycoside-polymixin-fluoroquinolone-amoxiclav-1st/2nd gen. cephalosporins respectively. Specific phenotypic testing for MRSA (cefoxitin) and MRSP (oxacillin) was rare in this population, but where it was carried out, it was negative.

The results indicated that although CoPS displaying a level of resistance is common, MDR would appear relatively rare in this population. It has previously been suggested that in dogs most CoPS isolates would be SP, which is generally noted for polymixin B susceptibility. However, in the current study, a large section of CoP isolates appeared to possess polymixin resistance. This may suggest a more important role for SA in this population of animals and presents a potential opportunity for further diagnostic speciation (Bannoehr, Guardabassi, 2012).

Update on previous reports.

This report briefly describes syndromic surveillance for gastrointestinal (GI) and respiratory disease conducted between 1st January and 30th June 2016, and compares it with previous years (Sánchez-Vizcaíno et al., 2015a; Sánchez-Vizcaíno et al., 2015b). The consultation rate for GI disease mostly decreased during the first 11 weeks of 2016 with a peak in week 1 (41 consultations per 1,000; Figure 2). The trend of respiratory disease was more stable, but still with an albeit more modest peak in week 1 (19 consultations per 1,000). The reported consultation rate for both GI disease and respiratory disease during the first semester of the current year (weeks 1 to 26) was lower compared to the rate for the same periods in 2014 and 2015; whether this represents a true change in disease or a change in the surveyed population characteristics as SAVSNET grows needs to be determined.

Update on MRSP

Staphylococcus pseudintermedius (SP; previously *S. intermedius*) is the most common CoPS of dogs and cats. It is both a mucosal commensal and an opportunistic pathogen and is the most common organism associated with canine pyoderma. MRSP isolates have recently emerged and spread in the USA (since

1999), Europe (since 2004) and the UK (since 2007), and are now considered worldwide. MRSP carries the *mecA* gene on a mobile element that may transfer horizontally between staphylococci. The *mecA* gene encodes an altered penicillin binding protein (PBP2a) and confers resistance to all beta-lactam antibiotics including potentiated amoxicillin and cephalosporins. MRSP usually show MDR; in addition to all beta-lactam antibiotics they are commonly resistant to aminoglycosides, macrolides, lincosamides, tetracyclines, trimethoprim, chloramphenicol and fluoroquinolones. Clindamycin resistance may be inducible during therapy, but this is usually tested in the laboratory.

Diagnosis: The diagnosis of staphylococcal pyoderma is made by cytology: degenerative neutrophils with intracellular coccoid bacteria in pairs or groups. The diagnosis of MRSP is made on culture and susceptibility testing. MRSP are phenotypically resistant to oxacillin, a marker for meticillin resistance (Clinical Laboratory Standards Institute 2004 breakpoints). Confirmation is by PCR for the *mecA* gene or latex agglutination testing for PBP2a. Most studies report low prevalence of MRSP carriage in healthy dogs (0-4.5%) and cats (1.2-4%). The reported prevalence of MRSP clinical isolates varies significantly geographically, but is generally increasing over time. In agreement with our early laboratory surveillance, the overall UK prevalence appears to be low (<20%), but higher prevalence is likely in referral practices. The carriage or infection risk increases with administration of antimicrobials, surgery, hospitalisation or frequent veterinary premises contact. Any patient with confirmed staphylococcal pyoderma and MRSP 'risk factors' should have culture and susceptibility testing performed to guide treatment and practice biosecurity.

MRSP outbreaks are possible with transfer and dissemination between patients, staff and their environment. Long-term canine carriage of MRSP (>1 year) following infection has been reported and may be prolonged by antibiotic treatment to which the bacterium is resistant. Staphylococcal strains can transfer between humans and pets, and vice versa. MRSP infections have been reported infrequently in immune-suppressed people, but MRSP detection in healthy people tends to be uncommon and transient. Transfer of MRSP between infected dogs and other household pets however is common. Furthermore MRSP can survive *in vitro* for extended periods (unpublished results) and positive environmental samples have been detected from veterinary premises even after routine cleaning. Biosecurity protocols are therefore needed to control the spread of such MDR bacteria within veterinary premises, with hand hygiene being the single most effective. Barrier nursing protocols can be implemented for suspected or identified cases. Mucosal (gingiva and perineal) swabbing may assist the epidemiological monitoring of MRSP-positive patients.

Investigation and treatment of the underlying disease is paramount for a successful outcome. Therapeutic options for treating MDR bacterial infections are severely limited and antibiotic therapy may further select for antibiotic resistance. Therefore, where possible, and particularly for superficial

pyoderma cases, topical therapy alone is recommended. The main topical antiseptic active against MRSP is 2-4% chlorhexidine. Veterinary products containing these ingredients are available in many forms (shampoo, sprays, wet wipes and mousse), improving compliance. Systemic antibiotics may be required to treat cases with severe/ widespread superficial pyoderma or deep pyoderma. If so, it is important to choose the correct antibiotic at the correct dose, frequency and duration for the individual case and use concurrent topical therapy. Treating MRSP pyoderma is challenging so seeking specialist advice may be recommended.

References

VAN DUIJKEREN, E., CATRY, B., GREKO, C., MORENO, M.A., POMBA, M.C., PYÖRÄLÄ, S., RUZAUSKAS, M., SANDERS, P., THRELFALL, E.J., TORREN-EDO, J., TÖRNEKE, K.; SCIENTIFIC ADVISORY GROUP ON ANTIMICROBIALS (SAGAM). (2011). Review on methicillin-resistant *Staphylococcus pseudintermedius*. Journal of Antimicrobial Chemotherapy 66, 2705-2714.

LAARHOVEN, L.M., DE HEUS, P., VAN LUIJN, J., DUIM, B., WAGENAAR, J.A., VAN DUIJKEREN, E. (2011). Longitudinal study on methicillin-resistant *Staphylococcus pseudintermedius* in households. PLoS One 6, e27788.

WINDAHL, U., REIMEGÅRD, E., HOLST, B.S., EGENVALL, A., FERNSTRÖM, L., FREDRIKSSON, M., TROWALD-WIGH, G., ANDERSSON, U.G. (2012). Carriage of methicillin-resistant *Staphylococcus pseudintermedius* in dogs--a longitudinal study. BMC Veterinary Research, 8: 34.

NIENHOFF, U., KADLEC, K., CHABERNY, I.F., VERSPOHL, J., GERLACH, G.F., SCHWARZ, S., KREIENBROCK, L., NOLTE, I., SIMON, D. Methicillin-resistant *Staphylococcus pseudintermedius* among dogs admitted to a veterinary teaching hospital. Veterinary Microbiology 2011; 150 (1-2), 191-197.

A global perspective on companion animal infection

Aujezkys disease, which is OIE reportable, was confirmed in a dog in the Czech Republic which was in contact with wild boar. Aujeszkys disease primarily infects pigs, but may be transmitted to other animal species including cats and dogs where it is usually fatal. While the disease is not present in the UK (last reported 2009), or many parts of Europe, foci of infection remain, especially in wild boar. People travelling with their pets to such areas should avoid contact with wild board and also not feed wild boar meat to their pets.

Babesia in UK. The distribution of canine babesiosis is largely driven by the habitat of its tick vector *Dermacentor reticulatus*. In the UK, these vectors were largely considered absent, such that canine babesiosis was sporadic and generally restricted to internationally-travelled animals. In February 2016, three cases of Babesia canis were reported in one Essex veterinary practice in dogs that had not travelled abroad. So far all available evidence suggests these home grown (autochthonous) cases in untravelled dogs are rare and associated with what currently appears to be a small pocket of *D. reticulatus* in the Chelmsford area. Real time updates on Babesia and other pathogens are available at www.savsnet.co.uk/realtimedata.

Rabbit haemorrhagic disease. Rabbit haemorrhagic disease virus (RHDV) type 1 has been endemic in the UK for many years and vaccines are available to protect pet and farmed species. More recently a new form of the virus RHDV-2 has been reported, initially in France in 2010, with the first UK cases in 2013. Although hard surveillance data is lacking, the virus appears to be spreading. The clinical signs vary from sudden death, to a more prolonged and progressive illness. Some rabbits appear to develop asymptomatic infections that may help spread infection. Unlike the original strain, RHDV-2 can also affect even very young rabbits. Field data suggests that at least some classic RHDV-1 vaccines fail to protect against RHDV-2. Vaccines against RHDV-2 are available elsewhere in the EU and may be imported under the Special Import Scheme (https://www.gov.uk/government/news/rabbit-haemorrhagic-disease-virus-type-2-vaccines).

Lyme disease. The PDSA reported in April an increase in the number of known and suspected cases of this important tick-transmitted disease that can affect dogs, less commonly cats, and also humans. Lyme disease is caused by *Borrelia* species (notably *Burgdorferi*) and is transmitted by *Ixodes* ticks. It is not transmitted from pet animals directly to their owners. Not all ticks carry *Borrelia*, and even when they do, not all bites transmit infection. Clinical signs can be vague, making clinical diagnosis hard. Whilst skin rashes in humans may be pathognomonic, laboratory testing and interpretation is complex. As a result, there remains a lot of uncertainty about the precise burden of disease in the UK. Vets might consider testing for Lyme disease in animals presenting with acute polyarthritis with recent tick exposure. When visiting areas where ticks are active, people should take steps to reduce tick bites, and promptly remove biting ticks (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/521829/Ticksandyourhealthinfoabouttickbites.pdf)

Conclusion

This is the third UK SADS report, which highlights the importance of pruritus in UK pet animals and the potential for MDR in canine CoPS. As we collect data for longer, our estimates of changes in disease burden will become more refined, allowing more targeted local and perhaps national interventions. Anonymised data can be accessed for research by contacting the authors. SAVSNET welcomes your feedback.

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References

SÁNCHEZ-VIZCAÍNO, F., JONES, P.H., MENACERE, T., HEAYNS, B., WARDEH, M., NEWMAN, J., RADFORD, A.D., DAWSON, S., GASKELL, R., NOBLE, P.J., EVERITT, S., DAY, M.J., MCCONNELL, K. (2015a). Small animal disease surveillance. Veterinary Record 177, 591-594.

SÁNCHEZ-VIZCAÍNO, F., DALY, J.M., JONES, P.H., DAWSON, S., GASKELL, R., MENACERE, T., HEAYNS, B., WARDEH, M., NEWMAN, J., EVERITT, S., DAY, M.J., MCCONNELL, K., NOBLE, P.J., RADFORD, A.D. (2015b). Small animal disease surveillance: respiratory disease. Veterinary Record 178, 361-364.

BANNOEHR, J., & GUARDABASSI, L. (2012). *Staphylococcus pseudintermedius* in the dog: taxonomy, diagnostics, ecology, epidemiology and pathogenicity. Veterinary Dermatology, 23(4), 253-e252.

RUSCHER, C., LÜBKE-BECKER, A., WLEKLINSKI, C.-G., ŞOBA, A., WIELER, L. H., & WALTHER, B. (2009) Prevalence of Methicillin-resistant *Staphylococcus pseudintermedius* isolated from clinical samples of companion animals and equidaes. Veterinary Microbiology, 136(1–2), 197-201.

Tables

Table 1. Percentage of treatments recommended in 15,527 dogs and 3,535 cats presenting with pruritus to veterinary practices in the UK. The same animal could be treated with more than one treatment per consultation.

Treatments	Number (%) of dogs	Number (%) of cats
None	985 (6.3)	190 (5.4)
Anti-parasitic	2,121 (13.7)	1,372 (38.8)
Topical antimicrobial	5,216 (33.6)	412 (11.6)
Systemic antimicrobial	4,065 (26.2)	867 (24.5)
Topical glucocorticoid	3,926 (25.3)	346 (9.8)
Systemic glucocorticoid	4,592 (29.6)	1,891 (53.5)
EFA supplements	411 (2.6)	43 (1.2)
Shampoo	1,669 (10.7)	30 (0.8)
Ear cleaner	1,881 (12.1)	133 (3.8)
Other treatments	2,799 (18.0)	368 (10.4)

Table 2. Percentage of canine CoPS isolates (n=184) that were tested for sensitivity against particular antibacterial classes, and the percentage of isolates displaying resistance to that particular class as percentage of all isolates tested.

Antibacterial Class	Number (%) of isolates tested	Number (%)isolates resistant
Amoxiclav	176 (100.0)	1 (0.6)
$1^{st}/2^{nd}$ gen. cephalosporins	176 (100.0)	2 (1.2)
Fluoroquinolones	176 (100.0)	8 (4.6)
Lincosamides	104 (58.9)	15 (8.6)
Extended-spectrum penicillins	97 (54.9)	67 (38.3)
Macrolides	90 (51.4)	12 (6.9)
Aminoglycosides	81 (46.3)	6 (3.5)
Polymixins	81 (46.3)	81 (46.3)
Tetracyclines	14 (8.0)	2 (1.2)
Amphenicols	6 (3.4)	1 (0.6)

Figures

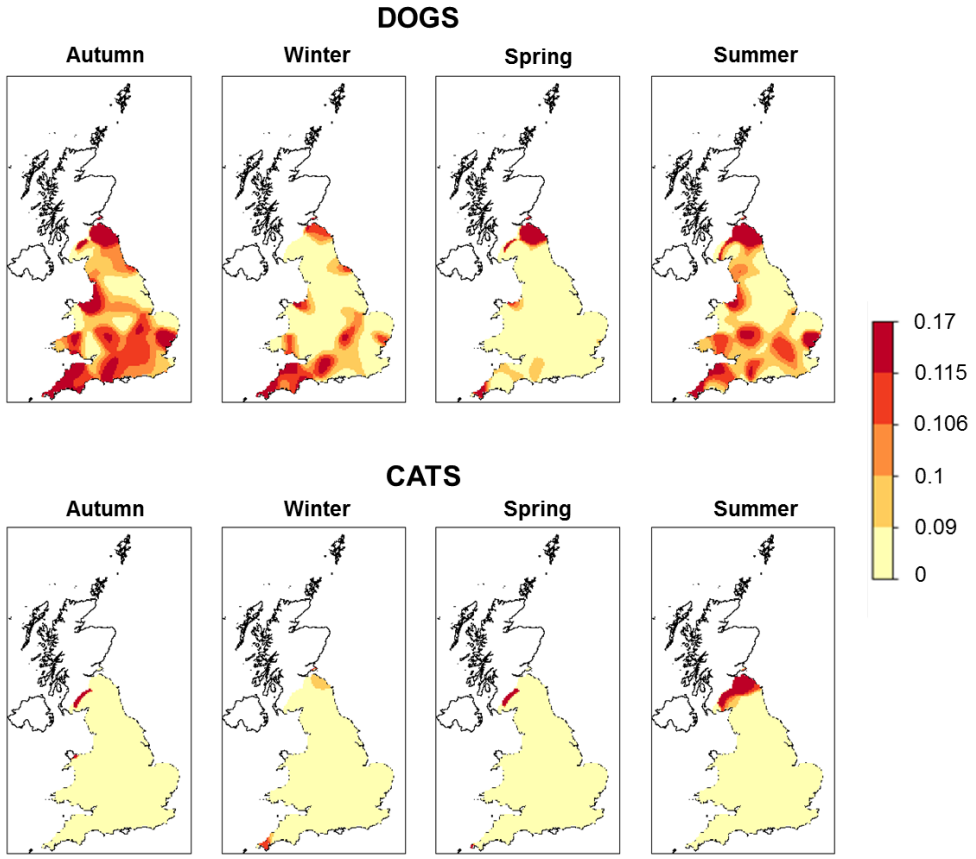

Figure 1. Kernel intensity ratio surface of England and Wales showing the relative risk of dogs and cats being presented with pruritus by season. The colours for relative risk have been categorised using the four cut-offs that divide the results obtained from dogs during autumn into five equal-size groups (quintiles) each containing 20% of all results.

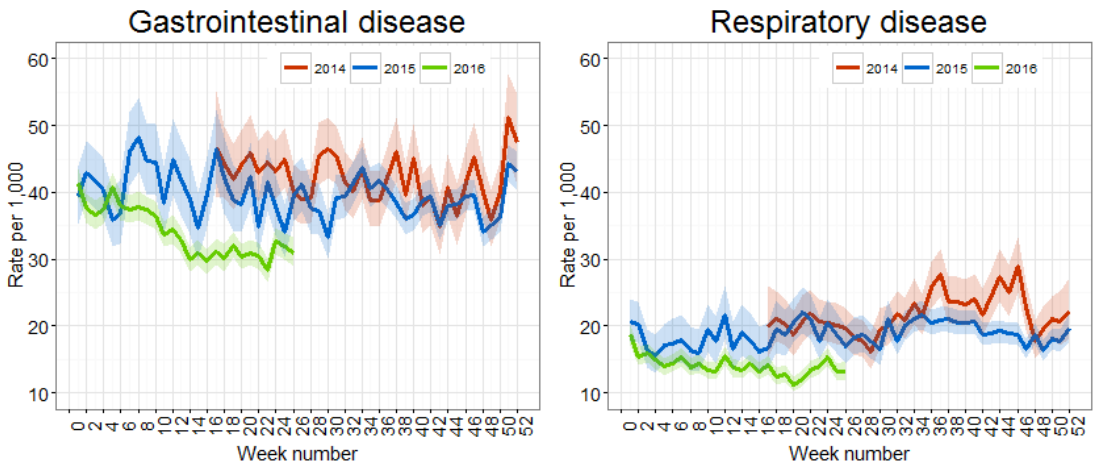

Figure 2. Weekly consultation rate for gastrointestinal disease and respiratory disease in a UK veterinary-visiting pet population between May 2014 and June 2016. The shaded areas around the solid lines depict the 95% confidence intervals for proportions calculated for each week.